

Driving Atmospheric Pressure Ion Sampling Efficiency to the MAX

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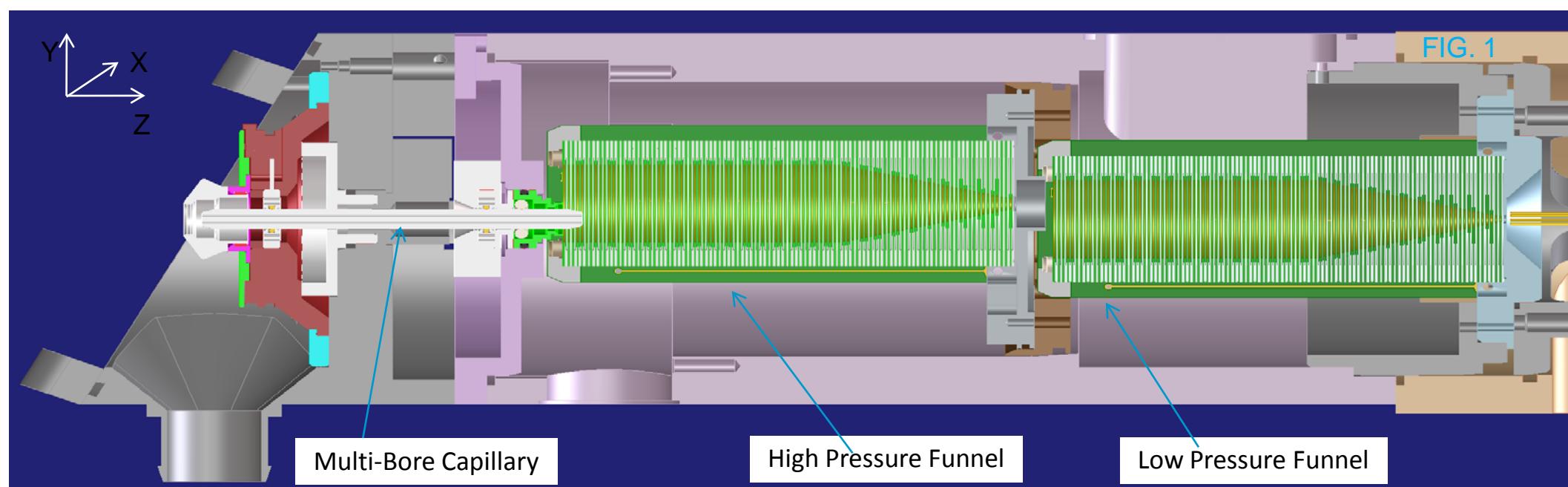
Introduction

Sensitivity and ion sampling efficiency for ESI ionization has been challenged over decades by several researchers primarily due to the significance for various analytical applications. One of the main challenges is ion transfer from atmospheric pressure into an MS device. In the present study, we report on coupling an ESI with thermal gradient focusing (Agilent Jet Stream™ - AJS) to an ion sampling inlet with a multi-bore ion sampling capillary followed by a dual ion funnel to efficiently transfer ions from atmospheric pressure into a mass analyzer. Ion sampling is studied and optimized theoretically and empirically with an objective to maximize ion collection efficiency from the atmospheric pressure region. The number of channels in a multibore capillary was varied for optimum ion collection. A few examples of LC/MS at conventional flow rates (~0.5 mL/min) and attogram detection limits are presented on the optimized system to illustrate the applications for the developed technology.

Experimental setup

MS

A novel API ion sampling interface was developed. The device consists of an orthogonal AJS ESI nebulizer with thermal gradient ion focusing confinement, 90mm hexa-bore resistive ion sampling capillary and dual differentially pumped ion funnel assembly (FIG. 1, 2, 3). This ion source and ion transfer optics configuration is referred to as the iFunnel. Ion funnels are made out of gold plated laminated conductors which are supported by printed circuit material to minimize electrical capacitance. The high pressure ion funnel operates at around 10 Torr [1], while the low pressure ion funnel operates at around 2 Torr. The iFunnel is coupled to the novel 6490 Agilent QQQ instrument. In this study we also used an AJS nebulizer which is movable along the axis of spraying (vertical, Y-axis) coupled to a 6460 Agilent QQQ mass spectrometer with a single bore ion sampling capillary to profile the spray plume in the direction of motion. An experiment was performed comparing sensitivity using capillaries with sampling bores (channels) from 1 to 7.



LC /MS- methods

Agilent 1290 LC

Column	ZORBAX Eclipse Plus C18, 2.1 x 50mm, 1.8 μm
Column temperature	ambient
Injection volume	1.0 mL
Autosampler temp	4 °C
Needle wash	flushport (methanol : water 75:25, 0.1% formic acid), 10 seconds
Mobile phase	A = 0.1% formic acid in water B = 0.1% formic acid in acetonitrile

MS conditions

	6490	6460
Gas temperature	150 °C	325 °C
Drying gas (nitrogen)	25 L/min	10 L/min
Nebulizer gas (nitrogen)	15 psi	20 psi
Sheath gas temperature	400 °C	400 °C
Sheath gas flow	12 L/min	12 L/min
Nozzle voltage	0 V	0 V
Capillary voltage	2500V	4000 V
MS1 and MS2 res	Unit	
Delta EMV	200 V	
Time Filtering	peak width 0.03 min	
Dwell time	200 ms	
Funnel voltages	DC = 15 V, ΔV1 = 180 V, ΔV2 = 100 V, RF (HP) = 200 V, RF (LP) = 110 V	

Experimental setup

FIG. 2

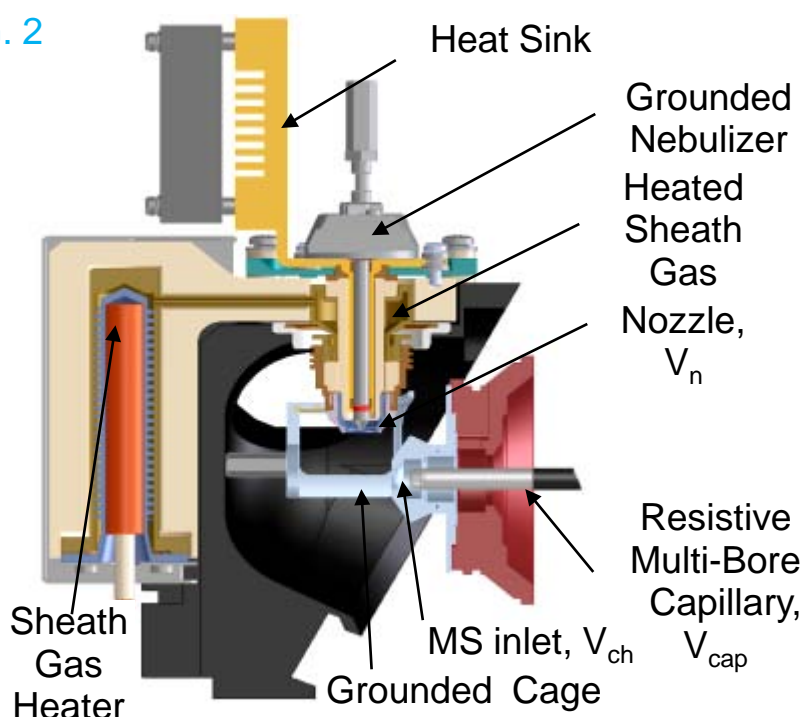
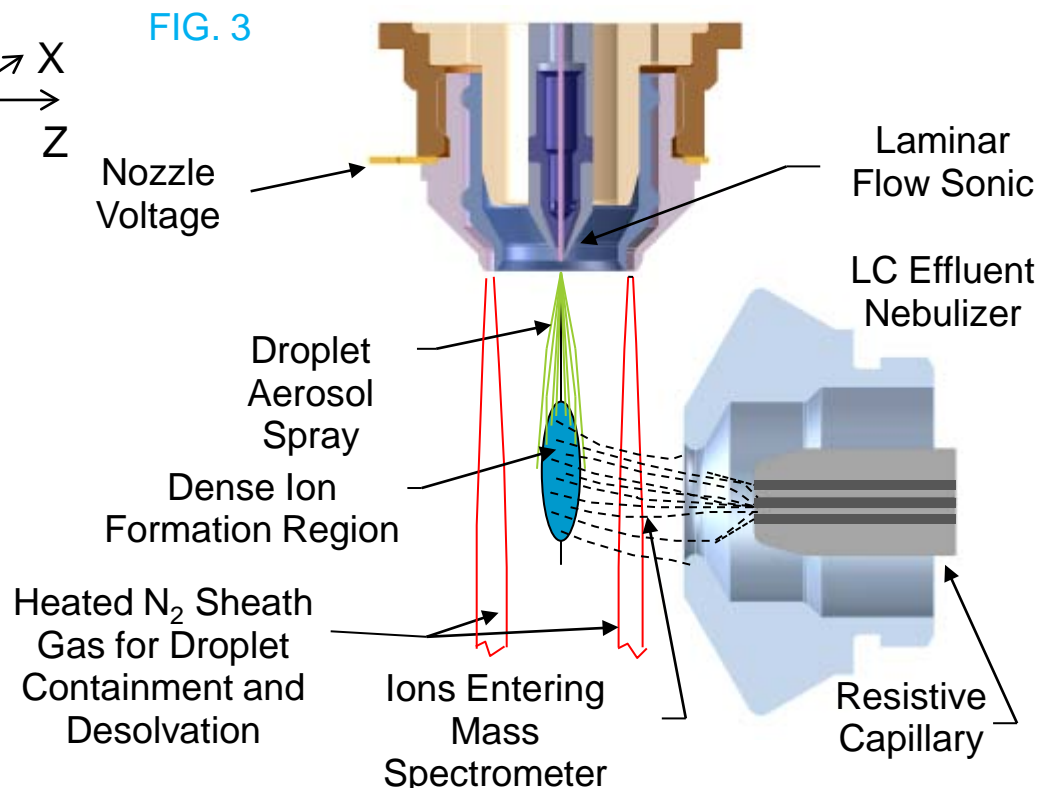


FIG. 3



Experimental results

It is important to know the spatial distribution of ions in the electrospray plume to optimize the location for the individual ion sampling channels within a multi-bore ion inlet for achieving the maximum ion sampling efficiency. Last year at the 57th ASMS Conference, we reported that AJS with 400 C sheath gas temperature results in electrospray plume confinement within a radial area limited to about 5mm in diameter. In this study, the axial distribution of ions within an ion plume for the AJS was characterized using a single bore capillary ion inlet by moving relative axial position for the AJS nebulizer vs. ion inlet. The data are presented on FIG. 4. According to these data, the axial distribution of ions has a characteristic length of about 15mm with an optimum transmission for different m/z values located at the coordinate origin (i.e. the standard location for the AJS vs. inlet in commercial 6460 and 6490 instruments).

FIG. 4 Ion Abundance vs. AJS location

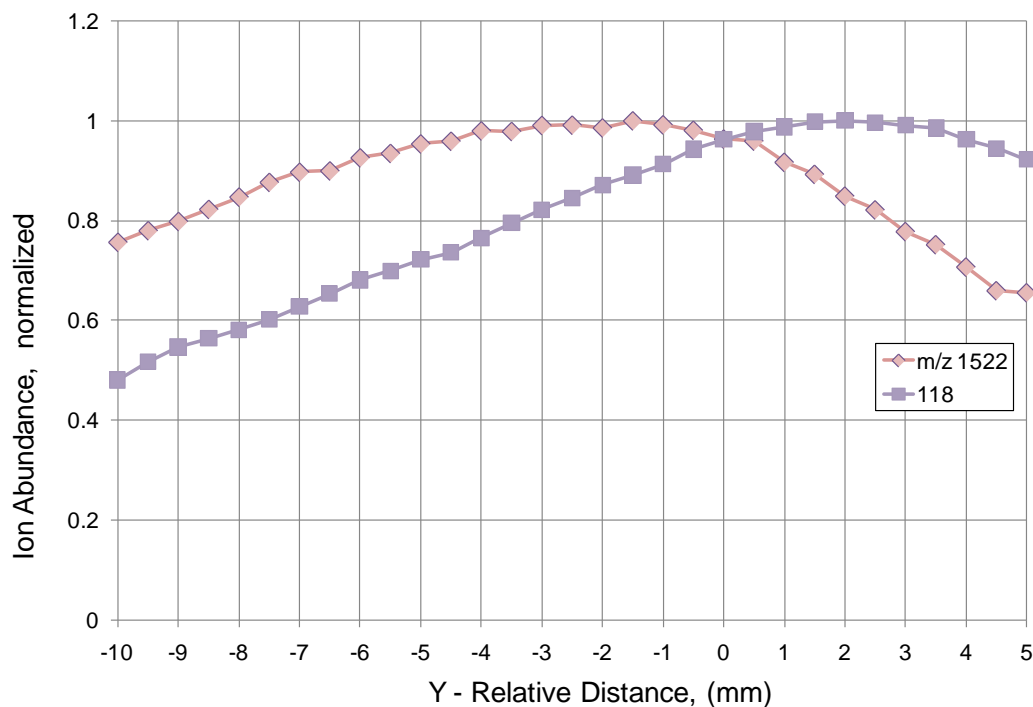
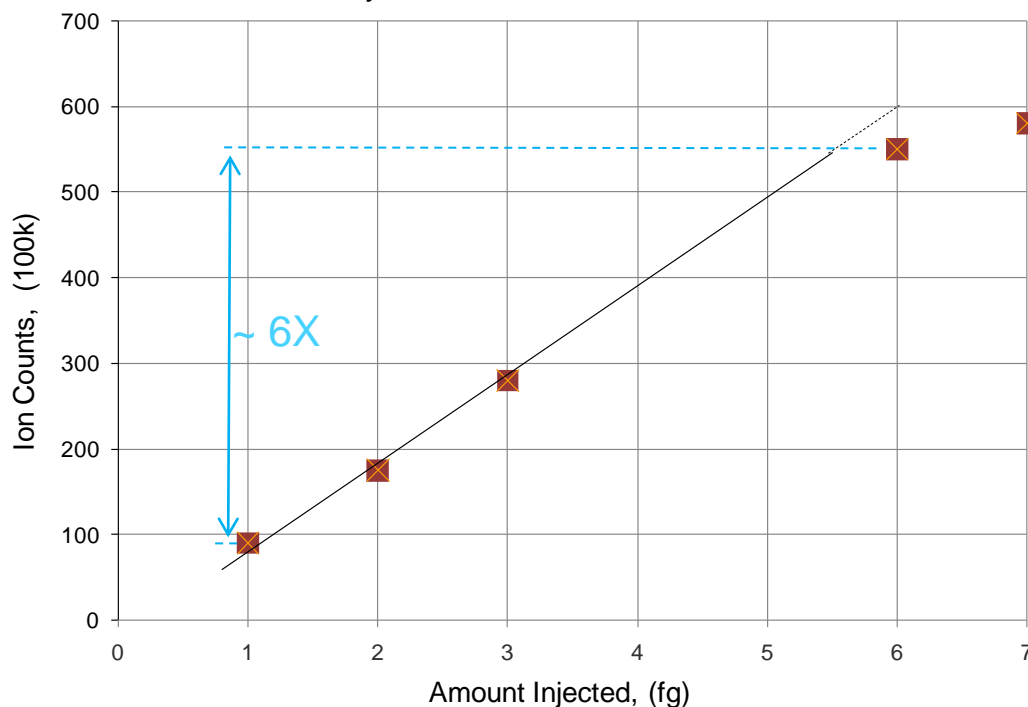


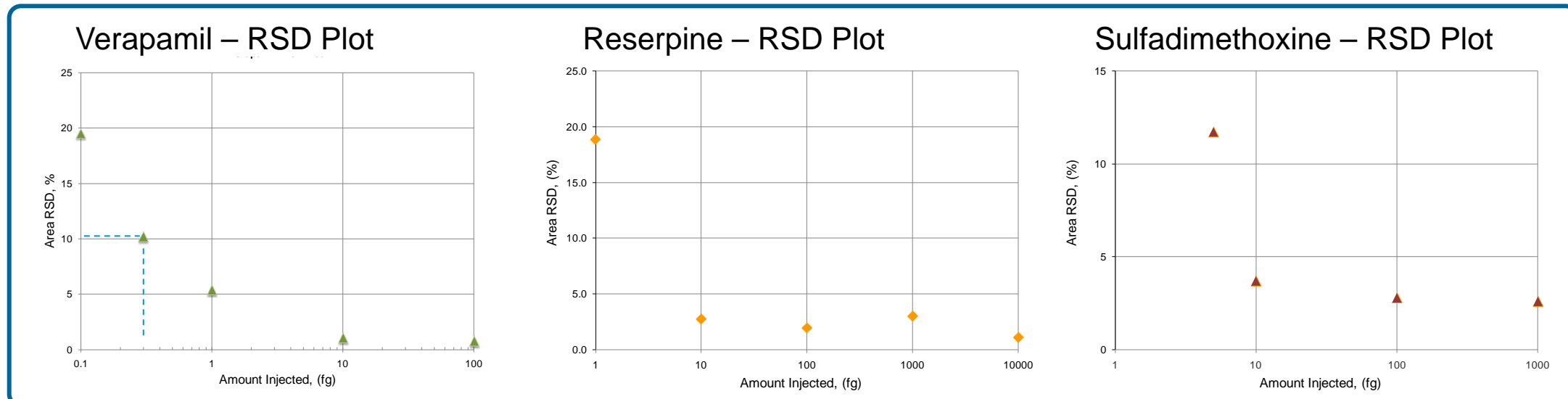
FIG. 5 Intensity vs. Number of Channels, $m/z=622$



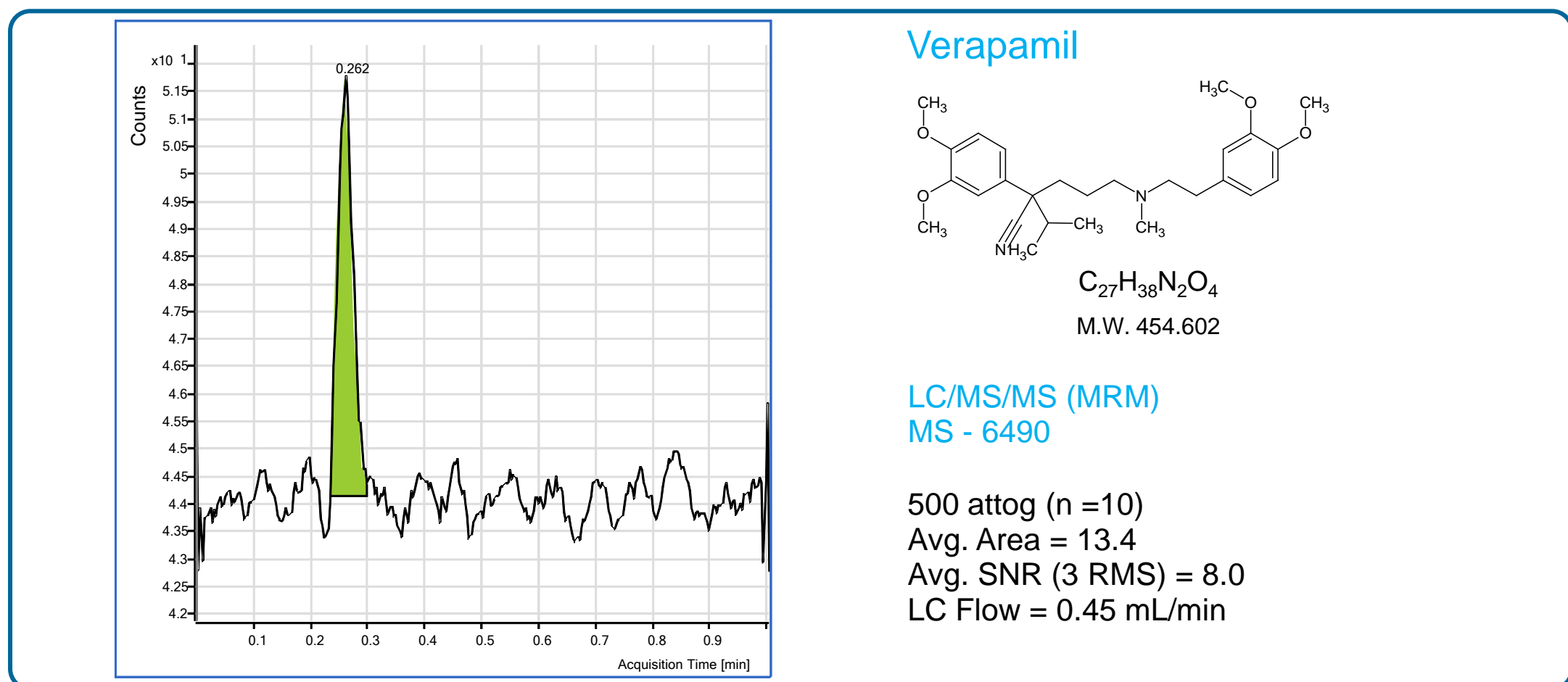
After the distribution of ions is known, the next optimization step is to find the locations for the individual multi-bore inlets that would result preferably in almost equal, additive and effective ion sampling for each individual channel. The FIG.5 shows data for 1, 2, 3, 6 and 7 individual 0.6 mm ID channels placed in a circular hexagon pattern with inscribed DIA of about 2mm and an identical center channel. In the experiment, it was possible to block individual channels by baffles to obtain ion collection from 1, 2, 3, 6 and 7 channels independently. The data illustrate that 6-channel hexagon arrangement acts near additively with respect to ion collection from individual channels, while adding the 7th center channel is less effective presumably due to the increased interaction and competition between channels. It is interesting to make a rough estimate for the ion collection efficiency Eff by dividing the total area of the projected plume, $5 \times 15mm^2$ which contains about 70% of the generated ions, by the ion sampling area of the multi-bore capillary with hexagon pattern, which can be estimated as a circle with about 5mm diameter:

$$Eff \sim 70\% * (\pi * 5^2 / 4) / (5 * 15) = 18\%$$

Experimental results



Another way to look at the efficiency of a mass spectrometer is to evaluate the ratio of the detected molecules to the total number of the consumed sample molecules. In this study, several pharmaceutical compounds were analyzed by LC/MS (MRM) to evaluate the increase in the peak area RSD values as a result of decreased amount of the sample where ion statistics play a dominant role, FIG.6. All experiments were performed on the optimized 6490 QQQ instrument with hexa-bore capillary and dual ion funnel. For compounds in FIG 6, RSD values of 10% correspond to about 100 ions detected and ion statistics are a dominant factor. Verapamil has the strongest ESI of the 3 studied drugs and 10% RSD is achieved at about 300 attograms (660 zeptomol), or 4×10^5 molecules, therefore resulting in the detection of 1 out of 4000 molecules of the sample. This is a quite remarkable result, since the commonly reported ratio for commercial API MS instruments is typically above 1 out of 10^5 ions. The ratio of the detected molecules drops for reserpine and sulfadimethoxine due to the lower proton affinity and the reduced ionization efficiency for these molecules. One of the representative chromatogram for verapamil is shown at FIG.7 to illustrate the results achieved at low levels.



Conclusions and References

Substantial improvements in ion sampling efficiency are achieved with the iFunnel Technology described in this paper, resulting in 1 out of 4000 sample molecules detected as ions using 6490 QQQ. Improvements of up to 6 times in ion collection efficiency at atmospheric pressure were obtained using the new hexa-bore ion sampling capillary and dual ion funnel. Attogram detection limits are demonstrated at conventional HPLC flow rates on the 6490 QQQ instrumentation equipped with iFunnel Technology.

[1] Scott A. Shaffer, Aleksey Tolmachev, David C. Prior, Gordon A. Anderson, Harold R. Udseth, and Richard D. Smith, *Anal. Chem.*, 1999, 71 (15), pp 2957–2964.